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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,320	06/12/2001	Ajay Hasmukhlal Upadhyay	RD 01022	5176

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
07/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/879,320	UPADHYAY, AJAY HASMUKHLAL	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 31-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 31-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment, remarks and declaration all dated 10-26-07 is acknowledged.

A request for suspension of action dated 10-26-07, for three months, was placed in file. Since the the three month period has expired the application is being acted upon.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-26-07 has been entered.

Claims 1-8 and 31-37 are pending in the instant application.

The following rejection is applied to the instant claims:

Claim Rejections - 35 USC § 103

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,372,252 to Blume et al (Blume) in view of US 5,032,406 to Dansereau et al (Dansereau), US 3627583 to Troy et al and Ansel et al (Pharmaceutical dosage forms).

Blume teaches immediate and sustained release formulations comprising guaifenesin. Blume teaches loading guaifenesin and methocel into a high shear mixer,

mixed at high speed, adding water and further mixing at additional time to complete granulation. The composition is next dried in fluid dryer and then passed through a mill fitted a suitable size screen (col. 7, lines 63 through col. 8, lines 23). Thus, the resulting material of Blume reads on agglomerated mixture because the processing of the material involves the same steps as described in the instant application.

Blume fails to teach granulation of guaifenesin with polyvinylpyrrolidone.

Dansereau teaches a tablet composition that provides dual action, for immediate and sustained release, comprising an outer tablet and an inner tablet respectively. The active ingredient of both inner and outer tablets comprises guaifenesin. The inner tablet particularly comprises guaifenesin and polyvinylpyrrolidone (PVP) (example I). Dansereau teaches that the inner tablet is made as follows (col. 6):

> The inner tablet is made by oscillating guaifenesin and half of the polyvinylpyrrolidone through a 30 mesh screen. The blend is then transferred to a pharmaceutical grade blender and mixed until it is of uniform consistency. It is then granulated with polyvinylpyrrolidone that had been previously dissolved in a sufficient amount of purified water to make a solution of from about 8% to about 12% of polyvinylpyrrolidone. This mixture is discharged and dried in a forced air oven at 40° C. until the water content is less than 1%. The dried granulation is then oscillated through a 12 mesh screen and returned to the blender. The remaining polyvinylpyrrolidone, microcrystalline cellulose and talc are added to this dried granulation and mixed until it is of uniform consistency. Finally, zinc stearate is added and the mixture is mixed until it is of uniform consistency. This mixture is then compressed into inner tablets using a standard tableting press.

Thus, the resulting inner tablet composition of Dansereau read on the claimed agglomerate mixture because the process involves the same steps as described in the instant specification (page 3, lines 15-20). Dansereau fails to teach the claimed particle sizes.

Troy teaches tablets formed by direct compression from a mixture of an active material such as therapeutic material and as a direct compression vehicle dry, free-flowing, granular sugar and a binder (abstract). Troy teaches that in order to obtain free-flowing particles of 12 mesh to 325 mesh (col. 1, L 50-65). Troy states that tablets result in good physical properties and readily dissolve in aqueous media (col. 1 and col. 4, L 1-10). Troy suggests mixing sugar and the binder to effect agglomeration of about 325 mesh (44 microns according to the declaration submitted by applicants on 10-26-07) but not greater than 12 mesh (col. 3, L 7-15 and lines 46-61). Among the active agents, Troy suggests antitussives but does not explicitly state employing guaifenesin.

Ansel et al teaches manufacturing of compressed tablet by different procedures such as wet granulation, dry granulation, and direct compression and states that the important requirement in tablet manufacture is a free-flowing drug from the hopper to the dies to enable high speed compression of powdered drug (page 209). In each of the types of compression tablet manufacture, Ansel teaches sizing the granules for free-flowing of drug and reduced capping (page 211, page 213 slugging and page 216). Ansel states that one reason for capping of tablets is the granulation which has too great a proportion of fines or fine powder (page 216, col. 2 and page 217).

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention from the teachings of Troy and Ansel that particle sizes of 12 mesh to 325 mesh are important for free flowing and the ability for compression, too fine a powder causes capping and while sizing of the granules particles is important for free flowing of drug. Ansel, Troy as well as Dansereau recognize PVP as a suitable binder for compressible tablets, particularly guaifenesin (Dansereau). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to employ PVP for the processing and preparation of compressible guaifenesin tablets of Blume because Ansel, Troy as well as Dansereau recognize PVP as a suitable binder and Dansereau recognizes methylcellulose (Blume) and PVP as equivalent binders as well as disintegrants in preparing a sustained release compressible tablet preparation comprising guaifenesin.

With respect to the claimed particle sizes, Blume teaches that no more than 30% granulation material passes through 100 mesh (150 microns) and not more than 10% retained on 10-mesh screen (greater than 850 microns). Thus, majority of the particles of Blume are in the range of 150 microns – 2 mm and a smaller percentage of particles are below 150 microns. A maximum of 30% of the particles that pass through the 100-mesh screen, according to Blume, could be any size below 150 microns (as low as 45 microns claimed in the instant invention). While Blume does not teach the exact percentages of particle sizes claimed in the instant application, there is an overlap in the particle sizes between instant application and that of Blume (150 nm to 425 nm). Instant claims (except for claims 7 and 35) do not state the distribution of particle sizes between

45 microns and 425 microns. On the other hand, Ansel suggests free flowing particles of appropriate size (not too fine a powder) that do not exhibit capping are important and Troy suggests a particle size of 12 mesh (1.41 mm) to 325 mesh (44 microns) as suitable for free flowing, stable and compressible tablets. Accordingly, a skilled artisan would have readily optimized the particle sizes of the granulated PVP and guaifenesin between 12 mesh and 325 mesh sizes such that the particles have an optimum flow rate, strength and stability and yet do not show capping.

For the claimed additives such as glidants, lubricants, silica, stearic acid etc., Blume and Dansereau teach the conventional excipients including lubricants such as magnesium stearate, calcium stearate etc; binders such as povidone (polyvinylpyrrolidone), gelatin, starch; glidants such as talc or silicon dioxide, stabilizers and other excipients such as lactose, sorbitol etc. Accordingly, in the absence of evidence to the criticality of the specific excipients and their amounts (claims 3-4 & 33-34), it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to the choose the appropriate excipient and optimize the amounts of the same in the composition of Blume with an expectation to achieve the desired effect.

Response to Arguments

3. Applicant's arguments filed 10-26-07 have been fully considered but they are not persuasive. While applicants primarily argue with respect to the teachings of Blume and

Dansereau, the present rejections are not made over Blume and Dansereau alone and instead over Blume, Dansereau, Ansel and Troy.

4. Applicants argue that Blume clearly does not teach the particle size limitations of the claimed composition and instead teaches 60% of his particle distribution lies within the range of 150-2000 microns. It is argued that whereas Blume permits 10% of his particles to be greater than 2000 microns, the claimed range restricts the composition such that only 30% is greater than 425 microns (425 micrometers). However, instant claims allow for at up to 30% to be higher than 425 microns, which could possibly include 10% particles having a size greater than 2000 microns. It is argued that in Blume about 30% of the granulation passes through a 100 mesh screen (150 microns) wherein in the claimed invention greater than 80% of the particles exhibit a particle size greater than about 45 microns (equivalent to a 325 mesh screen). However, the limitation that greater than 80% particles are above 45 microns does not explain what percentage particles are less than 150 microns and if all of the >80% of particles are between 45-150 microns. Given the upper limit of 425 microns and the limitations of claims 7 and 35 it is evident that only a portion (17% to 55%) of the particles between 45 microns and 425 microns possess a size of 45 to 150 microns. Therefore the argument that there is no indication that at least 80% would be retained on the 45 micron screen as instantly claimed is not persuasive. Besides, it can be reasonably argued that the 30% limitation with respect to the 100 mesh size in Blume reads on the 17-55% particles between 45 to 150 microns in the instant claims 7 and 35.

5. It is argued that the Examiner has expressly conceded that as Dansereau is cited only for the addition of PVP and not for its particle size any further discussion of Dansereau is necessary and that the proposed combination of Blume and Dansereau cannot possibly establish a prima facie case of obviousness for the claimed invention. Further, it is argued that because the claimed compositional properties also affect the performance properties of the composition, the limitations of Claim 31, cannot possibly be met by a particle size distribution as in Blume, as Blume has an unknown lower limit, and in which upper limit greatly exceeds the upper claimed size in the instant invention by orders of magnitude. Moreover, it is argued that Applicant's description of the prior art, page 2, lines 5-14 of the specification shows that prior art compositions had unacceptably high friability and unacceptably low hardness and tend to exhibit "capping", that is cracking and separation of part of the dosage form from the remaining body of the dosage form and it is further described at page 3 of the specification beginning at line 5 that the guaifenesin containing composition of the presently claimed invention provides improved robustness and flexibility with regard to processing conditions when the particle size distribution is such that less than about 30% by weight exhibit a particle size greater than about 425 micrometers and greater than about 80% by weight of the particles exhibit a particle size of greater than about 45 micrometers. However, as explained above, instant claims are not rejected over Blume and Dansereau and instead the new combination of references, particularly Troy and Ansel, emphasize the importance of particle size for free-flowing, compressing drug of good strength and the absence of capping.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611